UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/718,209	11/20/2003	Jeremy Guy Clarke	4-30827B	9043

1095 7590 02/08/2005

NOVARTIS
CORPORATE INTELLECTUAL PROPERTY
ONE HEALTH PLAZA 104/3
EAST HANOVER, NJ 07936-1080

EXAMINER	
HUI, SAN MING R	
ART UNIT	**PAPER NUMBER**
1617	

DATE MAILED: 02/08/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/718,209	CLARKE ET AL.	
	Examiner	Art Unit	
	San-ming Hui	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 November 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-20* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-20* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☒ Certified copies of the priority documents have been received in Application No. 09/930,337.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *2/10/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

This is a continuation of US Serial 09/930,337, filed 8/15/2001, which is a continuation of PCT/EP00/01270, filed 2/16/2000. the instant application also claims the benefits of Foreign application, United Kingdom 9903759.0, filed 2/18/1999.

Applicant's preliminary amendments filed November 20, 2003 have been entered.

Claims 1-20 are pending for examination.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1-10, 15-17, and 20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Akehurst et al. (US Patent 5,658,549 from the IDS received February 19, 2004) in view of O'Connor(from the IDS received February 19, 2004) and Tainsh et al. (WO 95/31964 from the IDS received February 19, 2004).

Akehurst et al. teaches an aerosol formulation of fluticasone propionate plus a β-agonist bronchodilator, salmeterol, comprising a propellant, a hydrogen-containing chlorofluorocarbon (See col. 2, line 2-8; also col. 8, line 44-55, Example 17). Akehurst et al. also teaches that the particle size suitable for inhalation as preferably in a range of 1-10 microns (See col. 2, line 32-37). Akehurst et al. teaches the weight ratio of fluticasone propionate to the β-agonist bronchodilator, salmeterol, as about 1:1.3 (See col. 8, line 44-55, Example 17). Akehurst et al. also teaches the fluticasone containing aerosol formulation is useful as the treatment of asthma (See col. 3, line 36-41). Akehurst et al. also teaches that 2 or more agents, which include formoterol, that are known to treat asthma can be combined in the aerosol composition (See col. 3, line 36-59). Akehurst also teaches that one of ordinary skilled in the art would be able to optimize the formulation by selecting appropriate salts or esters of the actives in order to formulate the aerosol composition (See col. 4, line 1-8).

Akehurst et al. does not expressly teach a composition comprising formoterol and fluticasone together. Akehurst et al. does not expressly teach the salt of formoterol as fumarate dihydrate. Akehurst et al. does not expressly teach the weight ratio of fluticasone propionate to the β-agonist bronchodilator as 1:5 to 1:50 or 1:10 to 1:25. Akehurst et al. does not expressly teach the composition be formulated into a nebulizable composition.

O'Connor teaches that employment of the combination of β-agonist and steroids in the management of asthma is more effective than that of either agent alone (See page 397, col. 2, last paragraph to page 398, col. 2, fourth paragraph). O'Connor also

teaches that the addition of β-agonist, salmeterol, to fluticasone regimen resulting in a greater improvement in asthma control than increasing the dose of fluticasone alone (See page 398, col. 1, last paragraph). O'Connor also teaches that formoterol, combining with a steroid compound, budesonide, in low dose would produce an equal effect as the high dose budesonide (See page 398, col. 2, second paragraph).

Tainsh et al. teaches a nebulizable composition of fluticasone propionate in an aqueous medium (water for injection) (See particularly page 3, line 20-30).

It would be obvious to one of ordinary skill in the art at the time the invention was made to substitute salmeterol for formoterol in the fluticasone composition and optimizing the weight ratio of fluticasone to formoterol herein. It would be obvious to one of ordinary skill in the art at the time the invention was made to select the herein claimed salt of formoterol as fumarate dihydrate. It would be obvious to one of ordinary skill in the art at the time the invention was made to formulate the instant formoterol-fluticasone composition as nebulizable composition.

One of ordinary skill in the art would have been motivated to substitute salmeterol with formoterol in the fluticasone composition and optimizing the weight ratio of fluticasone to formoterol herein because formoterol is known to augment the asthma control effectiveness of steroid compounds. Formoterol is also known to be useful in Akehurst et al.'s composition. The combination of β-agonist and steroid is known to be useful as asthma control. Therefore, based on Akehurst et al. and O'Connor, combining formoterol and fluticasone together in an aerosol composition would be reasonably expected to be effective in treating asthma. Furthermore, the optimization of result

effect parameters (e.g., amount and weight ratio of actives) is obvious as being within the skill of the artisan. Moreover, selecting one salt over the other would be obvious, based on Akehurst et al., to maximize the stability and compatibility of the agent.

One of ordinary skill in the art would have been motivated to formulate the instant formoterol-fluticasone composition as nebulizable composition since the nebulizable forms of fluticasone is known. Incorporating formoterol, an agent known for treating asthma when combining with a steroid, into the fluticasone-containing nebulizable composition of Snell using for the same purpose, i.e., treating asthma, would be prima facie obvious (See *In re Kerkhoven* 205 USPQ 1069).

Claims 1-6 and 11-20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Trofast (WO 98/31352, reference AM from the IDS received January 8, 2002) in view of O'Connor(reference AR from the IDS received January 8, 2002), references of record.

Trofast teaches a dry powder asthma treating composition comprising formoterol fumrate dihydrate and a steroid compound, such as fluticasone propionate (See abstract, page 2 line 8, also page 3, line 1-2). Trofast teaches the dry powder composition is in finely divided form (See page 2, line 26-27). Trofast also teaches the particle size suitable for inhalation as preferably in a range of 1-7 microns (See page 2, line 26-30). Trofast also teaches lactose is one of the suitable carriers for the dry powder formulation (See page 2, line 22; also page 7, line 1-13, Example 6). Trofast teaches the molar ratio between formoterol and the steroid compound, budesonide, as

1:555 to 2:1. Trofast also teaches the amount of formoterol fumarate dihydrate in the dry powder formulation as 3 to 30μg (See page 3, line 5-14). Trofast also teaches the dry powder formulation can be prepared by 5.2 parts of formoterol fumarate dihydrate, 798.8 parts of lactose, and 196 parts of buesonide (See page 7, line 15-19, Example 7).

Trofast does not expressly teach the dry powder composition comprising formoterol fumarate dihydrate with fluticasone propionate. Trofast does not expressly teach the ratio of formoterol fumarate dihydrate to budesonide as 1:5 to 1:50 or 1:10 to 1:25. Trofast does not expressly teach the weight ratio among formoterol fumarate dihydrate, budesonide, and the carrier as 3-36:25-500:4464-24972.

O'Connor teaches that employment of the combination of β-agonist and steroids in the management of asthma is more effective than that of either agent alone (See page 397, col. 2, last paragraph to page 398, col. 2, fourth paragraph). O'Connor also teaches that the addition of β-agonist, salmeterol, to fluticasone regimen resulting in a greater improvement in asthma control than increasing the dose of fluticasone alone (See page 398, col. 1, last paragraph). O'Connor also teaches that formoterol, combining with a steroid compound, budesonide, in low dose would produce an equal effect as the high dose budesonide (See page 398, col. 2, second paragraph).

It would be obvious to one of ordinary skill in the art at the time the invention was made to substitute fluticasone propionate for budesonide in the composition of Trofast and optimizing the weight ratio of fluticasone to formoterol and carrier herein.

One of ordinary skill in the art would have been motivated to substitute fluticasone propionate for budesonide in the composition of Trofast and optimizing the

weight ratio of fluticasone to formoterol and carrier herein because formoterol is known to augment the asthma control effectiveness of steroid compounds. Fluticasone propionate is also known to be useful in Trofast's composition. The combination of β-agonist and steroid is known to be useful as asthma control. Therefore, based on Trofast and O'Connor, combining formoterol and fluticasone together in a dry powder composition would be reasonably expected to be effective in treating asthma. Furthermore, the optimization of result effect parameters (e.g., amount and weight ratio of actives and carrier) is obvious as being within the skill of the artisan.

It is applicant's burden to demonstrate unexpected results over the prior art. See MPEP 716.02, also 716.02 (a) - (g). Furthermore, the unexpected results should be demonstrated with evidence that the differences in results are in fact unexpected and unobvious and of both statistical and practical significance. *Ex parte Gelles*, 22 USPQ2d 1318, 1319 (Bd. Pat. App. & Inter. 1992). Moreover, evidence as to any unexpected benefits must be "clear and convincing" *In re Lohr*, 137 USPQ 548 (CCPA 1963), and be of a scope reasonably commensurate with the scope of the subject matter claimed, *In re Linder*, 173 USPQ 356 (CCPA 1972). In the instant case, no data was demonstrated in the instant specification for evaluation of the unexpected benefits. Therefore, no unexpected results are seen to be present.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to San-ming Hui whose telephone number is (571) 272-

0626. The examiner can normally be reached on Mon 9:00 to 1:00, Tu - Fri from 9:00 to 6:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan, PhD., can be reached on (571) 272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

San-ming Hui
Primary Examiner
Art Unit 1617